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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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NANOSYS INC.
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EXAMINER	
NEGIN, RUSSELL SCOTT	
ART UNIT	**PAPER NUMBER**
1631	
MAIL DATE	**DELIVERY MODE**
06/11/2009	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/826,153	SCHER ET AL.	
	Examiner	Art Unit	
	RUSSELL S. NEGIN	1631	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *23 February 2009*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *26-37,40-42,44-48 and 60-63* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *26-37,40-42,44-48 and 60-63* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *3/30/2009*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Comments

Applicants' amendments and request for reconsideration in the communication filed on 23 March 2009 are acknowledged and the amendments are entered.

Claims 26-37, 40-42, 44-48, and 60-63 are pending and examined in this Office action.

Information disclosure statement

The information disclosure statement filed on 30 March 2009 has been considered. It is noted that the reference of Mahamuni et al. is a duplicate of the same reference already cited on a previous 892 form.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation

under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

The following rejection is reiterated and necessitated by amendment for new claims 62-63:

35 U.S.C. 103 Rejection #1:

Claims 26-29, 31-32, 34-35, 37, 40, 46-48, and 60-63 are rejected under 35 U.S.C. 103(a) as being unpatentable over Bruchez et al. [US Patent 6,274,323, issued August 14, 2001] in view of Mahamuni et al. [Journal of Applied Physics, 1999, volume 85, page 2861-2865].

Claim 26 is drawn to a composition comprising a population of nanocrystals characterized by an excitation spectrum and an emission spectrum, wherein the emission spectrum and at least a portion of the excitation spectrum are in the nonvisible range; wherein the population of nanocrystals comprises a mixture of two or more subsets of nanocrystals, the subsets characterized by different excitation wavelengths; and wherein the emissions of the population comprise different wavelengths or different wavelength intensities when alternately excited with different excitation wavelengths.

The patent of Bruchez et al. uses semiconductor nanocrystals as detectable labels in various chemical and biological species.

Specifically, the abstract of Bruchez et al. states:

> The use of semiconductor nanocrystals as detectable labels in various chemical and biological applications is disclosed. The methods find use for detecting a single analyte, as well as multiple analytes by using **more than one semiconductor nanocrystal as a detectable label, each of which emits at a distinct wavelength**. (emphasis added by examiner)

Consequently, since Bruchez et al. teaches "more than one semiconductor nanocrystal as a detectable label, each of which emits at a distinct wavelength," Bruchez et al. teaches a plurality (i.e. mixture) of different nanocrystals.

Bruchez et al. comprises semiconductor nanocrystals producing emissions in the nonvisible spectra in column 17, lines 30-32 and column 20, lines 28-33, which states, respectively:

> Finally, semiconductor nanocrystals that emit energy in the blue to near ultraviolet include, but are not limited to ZnS and GaN.

> Likewise, for semiconductor nanocrystals producing emissions in the infrared or ultraviolet regions, the characteristic wavelengths that the discrete optical transitions occur at provide information about the identity of the particular semiconductor nanocrystal, and hence about the identity of or location of the analyte of interest.

Consequently, the nanocrystals of Bruchez et al. comprise nanocrystal populations with nonvisible emissions spectra.

Bruchez et al. also comprises semiconductor nanocrystal populations having portions of the spectra in the nonvisible range (see column 5, lines 9-15):

> In addition, the range of excitation wavelengths of such nanocrystals is broad and can be higher than the emission wavelengths of all available semiconductor nanocrystals. Consequently, this allows the use of a single energy source, such as light, to effect simultaneous excitation of all populations of semiconductor nanocrystals in a system having distinct emission spectra.

Consequently, the nanocrystals of Bruchez et al. comprise nanocrystal populations with portions of nonvisible excitation spectra.

Bruchez et al. does not teach that emissions of the population comprise different wavelengths or different wavelengths intensities when alternately excited with different excitation wavelengths.

The article of Mahamuni et al. studies spectroscopic and structural characterization of electrochemically grown ZnO quantum dots.

Specifically, Figures 5 and 6, when taken together, illustrates the alternating excitation of ZnO quantum dots using excitation wavelengths of 300 nm and 325 nm, respectively.

Claim 27 is further limiting with the additional limitation of the nanocrystal being a semiconductor nanocrystal.

Claim 28 is further limiting wherein the nanocrystal further comprise a diameter ranging from about 1000 nm to about 0.1 nm.

Claim 29 is further limiting wherein the nanocrystal further comprises a diameter ranging from about 50 nm to about 15 nm.

The term "semiconductor nanocrystal" is defined in column 8 of Bruchez et al., lines 59-65:

> The terms "semiconductor nanocrystal," "quantum dot," and "QdotTM nanocrystal" are used interchangeably herein and refer to an inorganic crystallite between about 1 nm and about 10000 nm in diameter or any integer or fraction of an integer therebetween, preferably between about 2 nm and about 50 nm…

Consequently, Bruchez et al. teaches the required properties of nanocrystal type and size.

Claim 31 is further limiting wherein the coated nanocrystals comprise an inner core, and the coating layer of the semiconductor comprises a band gap greater than that of the core.

Claim 32 is further limiting wherein the nanocrystals comprise InP.

Claim 34 is further limits the nanocrystal composition to comprise two or more sets of nanocrystals with differing emission wavelengths.

Claim 35 is further limiting wherein the additional limitation of restricting the spectral line widths.

Claim 37 is further limiting wherein the additional limitation of the excitation spectrum comprising ultraviolet, visible, or infrared wavelengths.

Claim 38 is further limiting wherein the additional limitation of comprising two or more sets of nanocrystals with differing excitation wavelengths.

Claim 40 is further limiting wherein the emission spectrum comprises nonvisible wavelengths.

Bruchez et al. teaches InP in column 9, line 16.

On the subject of spectral widths and bandgaps energies, Bruchez et al. states in column 18, lines 1-5 and lines 19-23:

> However, for some applications high information density will not be required and it may be more economically attractive to use more polydisperse particles. Thus, for applications that do not require high information density, the linewidth of the emission may be in the range of 40-60 nm...
>
> Suitable materials for the overcoating layer include semiconductor materials having a higher bandgap energy than the semiconductor nanocrystal core.

The use of multiple populations of nanocrystals is described in column 19 lines 23-26 of Bruchez et al.

> The above method can be used to prepare separate populations of semiconductor nanocrystals, wherein each population exhibits a different characteristic photoluminescence spectrum.

Consequently, Bruchez et al. produces separate populations of semiconductor nanocrystals with each population having a specified and unique photoluminescence spectrum.

As discussed above, the emission spectra of the nanocrystals comprise nonvisible wavelengths.

Claim 46 is further limiting wherein the adherent matrix comprises a polymer.

Claim 47 is further limiting wherein the composition is excitable or detectable through a barrier.

Claim 48 is further limiting wherein the barrier comprises animals.

Claim 60 is further limiting wherein the additional limitation that the population of nanocrystals linked to an adherent matrix, which adherent matrix comprises an affinity molecule of an antibody.

Claim 61 is drawn to an object tagged with the composition of claim 26.

Bruchez et al. states that polymers or animals can be used as detectable barriers for the semiconductor nanocrystals.

The patent of Bruchez et al. uses semiconductor nanocrystals as detectable labels in various chemical and biological species. Bruchez et al. discloses using the nanocrystals as adherents to several types of biopolymer in column 22, line 62 to column 23, line 5, which states:

> For example, the semiconductor nanocrystals of the present invention can readily be functionalized to create styrene or acrylate moieties, thus enabling the incorporation of the semiconductor nanocrystals into polystyrene, polyacrylate or other polymers such as polyimide, polyacrylamide, etc …

Consequently, the polymers or biopolymers are the affinity molecules and objects tagged with the nanocrystals.

Bruchez et al. continues on column 23, lines 50-60 by explaining that the semiconductor nanocrystals can be used in animals in which animals themselves are the barriers.

With regard to claims 62-63, Bruchez et al. also discloses nanocrystal mixtures in column 8, lines 45-50. Bruchez et al. discloses using the nanocrystals adhered to several types of biopolymer in column 22, line 62 to column 23, line 5, which states:

> For example, the semiconductor nanocrystals of the present invention can readily be functionalized to create styrene or acrylate moieties, thus enabling the incorporation of the semiconductor nanocrystals into polystyrene, polyacrylate or other polymers such as polyimide, polyacrylamide, etc …

Bruchez et al. continues in column 22, lines 23-35 by explaining how matrices and solid supports have the benefit of improved solubility and performance of the linked nanocrystals.

It would have been obvious to someone of ordinary skill in the art at the time of the instant invention to modify the nanocrystals that adhere to polymers of Bruchez et al. by use of the alternating excitation wavelengths of light in Mahamuni et al. wherein

the motivation would have been that Mahamuni et al. alternates between two excitation wavelengths and results in more informative spectra that display features of the quantum dots in one wavelength that are not present in the other wavelength [i.e. see Figures 5-6 of Mahamuni et al.]. There would have been a reasonable expectation in combining the references because not only does Bruchez et al. and Mahamuni et al. pertain to analogous subject matter of quantum dots and nanocrystals, but additionally Figure 5 and 6 of Mahamuni et al. demonstrate a general concept of using alternate wavelengths (i.e. 325 nm vs. 300 nm) applicable to the quantum dot/nanocrystal mixtures of Bruchez et al.; the ZnO of Mahamuni et al. is analogous to the ZnS nanocrystals studied in Bruchez et al.

Response to Arguments:

Applicant's arguments filed 23 February 2009 have been fully considered but they are not persuasive.

In response to arguments regarding the Pre-appeal Conference Request of 9/12/08, it is noted that the rejections of record argued in the Request were withdrawn in the Nonfinal office action mailed 12/23/08, and new rejections citing a new combination of references were made. Applicants arguments that "Applicants won a Decision that found the rejections improper based on arguments presented that the cited references do not teach mixed populations of nanocrystals" is incorrect. The "decision" mailed 10/21/08 merely stated that a rejection would be withdrawn and did not provide any indication of which of the several arguments presented in the pre-appeal conference

request were found persuasive. It is noted that the pre-appeal conference request delineated four arguments. The fourth argument, from page 4 of the request, stated, "claim 26 is additionally not obvious for failure of the Actions to cite a reference teaching of the claim limitation "wherein the emissions of the population comprise different wavelengths or different wavelength intensities when alternately excited with the different excitation wavelengths". " The office action of 12/23/08 explicitly stated on page 5 that **"Bruchez et al. does not teach that emissions of the population comprise different wavelengths or different wavelengths intensities when alternately excited with different excitation wavelengths**," and that statement is reiterated in the rejection above, thus making it clear on the record which argument was found persuasive and why the prior art of Mahamuni et al. was newly cited.

It is further noted that the first three arguments presented in the pre-appeal conference request were fully addressed on pages 9-10 of the office action mailed 12/23/08 wherein reasons were provided for why those arguments were not found persuasive.

Applicant argues that the "semiconductor nanocrystal" of Bruchez. et al. only includes a mixture of two or more of the same type of semiconductor nanocrystals because Bruchez et al.'s description includes a standard "boilerplate" statement used to encompass a mixture of two or more of the ***same*** type of nanocrystal molecules. This argument is not persuasive because the composition, in light of the other cited passages and language of the specification of Bruchez et al., [i.e. column 8, lines 43-50 and column 9, lines 11-18], is a mixture of semiconductor nanocrystals encompassing

different species of nanocrystals. Furthermore, the abstract, as reiterated below states:

> The use of semiconductor nanocrystals as detectable labels in various chemical and biological applications is disclosed. The methods find use for detecting a single analyte, as well as multiple analytes by using **more than one semiconductor nanocrystal as a detectable label, each of which emits at a distinct wavelength**. (emphasis added by examiner)

Consequently, since Bruchez et al. teaches "more than one semiconductor nanocrystal as a detectable label, each of which emits at a distinct wavelength," Bruchez et al. teaches a plurality (i.e. mixture) of different nanocrystals.

Further, applicant has provided no evidence as to why the two or more nanocrystals are necessarily the same type of nanocrystals, and as the remainder of the document of Bruchez et al. refers to a plurality of different types of nanocrystals, Bruchez et al. is reasonably interpreted to encompass a plurality of DIFFERENT nanocrystals and is not interpreted to be "boilerplate". Applicant additionally argues on pages 9-10 of the Remarks that Mahamuni et al. does not overcome this alleged deficiency in the prior art. This argument is not persuasive because as discussed above, Bruchez et al. teaches a mixture of a population of different nanocrystals.

Applicant next argues that there is no reasonable expectation of the success for the references of Bruchez et al. and Mahamuni et al. to function predictably with one another. Specifically, applicant argues that even assuming that Bruchez et al. teaches a mixture of different nanocrystals, then this mixture would have interactions which constitute a different function resulting in a different ultimate emission output compared to the separate nanocrystals taught in Mahamuni et al. This argument is not persuasive, and the reasonable expectation of success is reiterated below:

There would have been a reasonable expectation in combining the references because not only does Bruchez et al. and Mahamuni et al. pertain to analogous subject matter of quantum dots and nanocrystals, but additionally Figure 5 and 6 of Mahamuni et al. demonstrate a general concept of using alternate wavelengths (i.e. 325 nm vs. 300 nm) applicable to the quantum dot/nanocrystal mixtures of Bruchez et al.; the ZnO of Mahamuni et al. is analogous to the ZnS nanocrystals studied in Bruchez et al.

The following rejection is reiterated:

35 U.S.C. 103 Rejection #2:

Claims 33, 36, and 41-42 are rejected under 35 U.S.C. 103(a) as being unpatentable over Bruchez et al. in view of Mahamuni et al. as applied to claims 26-29, 31-32, 34-35, 37, 40, 46-48, and 60-63 above, and further in view of Cao et al. [Angew. Chem. Int. Ed., 1999, volume 38, pages 3692-3693].

Claim 33 is further limiting wherein the coating layer comprises CdSe.

Claim 36 is further limiting wherein the nanocrystals are those manufactured by colloidal synthesis.

Claim 41 is further limiting wherein a subset of the nanocrystals comprises a predetermined intensity of emission at a wavelength.

Claim 42 is further limiting wherein the intensity is predetermined by varying the concentration of a nanocrystal constituent, the presence of an overcoating, or by varying representation of the nanocrystal subset.

Bruchez et al. and Mahamuni et al. make obvious the composition of nanocrystals, as discussed above.

Bruchez et al. and Mahamuni et al. do not teach use of CdSe as a coating, or colloidal synthesis.

As the title of Cao indicates, one of the crystal coatings used is CdSe.

Columns 1 and 2 of pages 3694 of Cao et al. describe the colloidal synthesis process of the nanocrystals.

Cao et al. teaches that the crystals emit at "determined" wavelengths and intensities; consequently, the predetermined intensity of emission is a property illustrated in Figure 1 of Cao et al. as a function of the overcoating on the nanocrystal subset representation.

It would have been obvious to someone of ordinary skill in the art at the time of the instant invention to modify the nanocrystals that adhere to polymers of Bruchez et al. and the alternating excitation wavelengths of light in Mahamuni et al. by use of the spectra that varies in a predetermined manner based on nanocrystal size as in Cao et al. wherein the motivation would have been that the predetermined spectral profile in Figure 1 of Cao et al. demonstrates a reference by which to verify size distributions of nanocrystals. It would have been further obvious to one of ordinary skill in the art at the time of the instant invention to modify the nanocrystal systems of Bruchez et al. by using a CdSe coated nanocrystal as in Cao et al. because it is obvious to try known elements in the prior art to yield a predictable result. In this instance, CdSe coated InAs nanocrystals are an alternate form of nanocrystals used to obtain excitation and emission spectra. There would have been a reasonable expectation of success in using the species of CdSe coated nanocrystals because the methods of Bruchez et al. are generally applicable to semiconductor nanocrystals such as CdSe.

Response to Arguments:

Applicant's arguments filed 23 February 2009 have been fully considered but they are not persuasive.

Applicant argues that the additional reference does not overcome the alleged deficiencies of the first 35 U.S.C. 103 Rejection. As set forth above, the cited combination of references of Bruchez et al. and Mahamuni et al. teaches all of the limitation of the claims, therefore this argument is not persuasive.

The following rejection is reiterated:

35 U.S.C. 103 Rejection #3:

Claims 44-45 are rejected under 35 U.S.C. 103(a) as being unpatentable over Bruchez et al. in view of Mahamuni et al. as applied to claims 26-29, 31-32, 34-35, 37, 40, 46-48, and 60-63 above, and further in view of Weiss et al. [WO 00/55631].

Claim 44 is further limiting in that the population of nanocrystals comprises a predetermined excitation spectra or emission spectra.

Claim 45 is further limiting by varying the size of the nanocrystal.

Bruchez et al. and Mahamuni et al. make obvious the composition of nanocrystals, as discussed above.

Bruchez et al. and Mahamuni et al. do not teach a predetermined excitation or emission spectra by varying size of the nanocrystals.

The patent of Weiss et al. investigates nanocrystal probes for biological applications and states on page 14, lines 14-20:

> Furthermore, the frequency and wavelength of the narrow wavelength band of light emitted form the semiconductor nanocrystal may be further selected according to the physical properties, such as size, of the semiconductor nanocrystal. The wavelength band of light emitted by the semiconductor nanocrystal, formed using the above embodiment, may be determined by either (1) the size of the core, or (2) the size of the core and the size of the shell...

Consequently, the limitations of varying the size of the nanocrystal to produce a determined excitation or emissions spectrum are addressed.

On page 15, lines 5-12, Weiss et al. states, "Selection of the emission wavelength by varying the composition, or alloy, of the semiconductor nanocrystal is old in the art. As an illustration, when CdS semiconductor nanocrystal, having an emission wavelength of 400 nm, may be alloyed with a CdSe semiconductor nanocrystal, having an emission wavelength of 530 nm."

On page 53, lines 12-28, Weiss et al. explains the advantages of using their semiconductor nanocrystals:

> Thus, the invention provides an semiconductor nanocrystal probe containing a semiconductor nanocrystal capable, upon excitation by either electromagnetic radiation (of either narrow or broad bandwidth) or particle beam, of emitting electromagnetic radiation in a narrow wavelength band and/or absorbing energy and/or scattering or diffracting said excitation, thus permitting the simultaneous usage of a number of such probes emitting different wavelengths of electromagnetic radiation to thereby permit simultaneous detection of the presence of a number of detectable substances in a given material. The probe material is stable in the presence of light or oxygen, capable of being excited by energy over a wide spectrum, and has a narrow band of emission, resulting in an improved material and process for the simultaneous and/or sequential detection of a number of detectable substances in a material such as a biological material.

Consequently, the advantage of the technique of Weiss et al. is simultaneous detection of a number of detectable substances in a biological material.

It would have been obvious at the time of the instant invention for someone of ordinary skill in the art to modify the compositions of Bruchez et al. and Mahamuni et al. by use of Weiss et al. wherein the motivation would have been that Weiss et al. has the advantage of detecting multiple substances simultaneously using a given wavelength of excitation relevant to biological applications [see page 53, lines 12-28 of Weiss et al.].

Response to Arguments:

Applicant's arguments filed 23 February 2009 have been fully considered but they are not persuasive.

Applicant argues that the additional reference does not overcome the alleged deficiencies of the first 35 U.S.C. 103 Rejection. As set forth above, the cited combination of references of Bruchez et al. and Mahamuni et al. teaches all of the limitation of the claims, therefore this argument is not persuasive.

The following rejection is reiterated:

35 U.S.C. 103 Rejection #4:

Claim 30 is rejected under 35 U.S.C. 103(a) as being unpatentable over Bruchez et al. in view of Mahamuni et al. as applied to claims 26-29, 31-32, 34-35, 37, 40, 46-48, and 60-63 above, and further in view of Bruchez et al. [Science, volume 281, 1998, pages 2013-2016, Information Disclosure Statement, source CA, 19 October 2004]. This second Bruchez reference will be referred to as "Bruchez et al. (1998)."

Claim 30 is further limiting with the additional limitation that the production of the nanocrystals employs the usage of substitutes silanes.

Bruchez et al. and Mahamuni et al. make obvious the composition of nanocrystals, as discussed above.

Bruchez et al. and Mahamuni et al. do not teach use of substituted silanes.

The article of Bruchez et al. (1998) investigates semiconductor nanocrystals as fluorescent biological labels and states in the abstract:

> Semiconductor nanocrystals were prepared for use as fluorescent probes in biological staining and diagnostics. Compared with conventional fluorophores, the nanocrystals have a narrow, tunable, symmetric emission spectrum and are photochemically stable. The advantages of the broad, continuous excitation spectrum were demonstrated in the dual emission, single excitation labeling experiment on mouse fibroblasts. These nanocrystal probes are thus complementary and in some cases may be superior to existing fluorophrores.

Consequently, Bruchez et al. (1998) investigates semiconductor nanocrystals with dual emission in mouse fibroblasts.

Bruchez et al. (1998) ends the article by stating:

> The development of nanocrystals for biological labeling opens up new possibilities for many multicolor experiments and diagnostics. Further, it established a class of fluorescent probe for which no small organic molecule equivalent exists. The tunability of the optical features allows for their use as direct probes or as sensitizers for traditional probes. These nanocrystals have long fluorescent lifetimes (hundreds of nanoseconds), which can allow for time-gated detection for autofluorescence suppression. Further development, such as direct immunolabeling, in situ hybridization, and incorporation into microspheres will be important for applications such as cytometry and immunocytobiology. In addition nanocrystal probes may prove useful for other contrast mechanisms such as x-ray fluorescence, x-ray absorption, electron microscopy, and scintillation proximity imaging, and the use if for-red or infrared-emitting nanocrystals (InP and InAs) as tunable, robust infrared dyes is another possibility.

Consequently, there are advantages of using nanocrystals in biological applications.

Footnote number 20 on page 2015 of Bruchez et al. (1998) shows how the nanocrystals are synthesized using substituted silanes and the formation of polymers (footnotes 20 and 22). Use of silanes is a widely accepted procedure for generating nanocrystals.

It would have been obvious to someone of ordinary skill in the art at the time of the instant invention to modify the compositions of Bruchez et al. and the alternating wavelengths of Mahamuni et al., by use of the substitutes silanes of Bruchez et al. (1998) wherein the motivation would have been that Bruchez et al. (1998) has the advantage of improving a common technique in the art (use of silanes to make nanocrystals) to generate the nanocrystals with tunable wavelengths; this improvement results in better performance of biological measurement techniques (i.e. X-ray fluorescence, x-ray absorption, and scintillation proximity imaging).

Response to Arguments:

Applicant's arguments filed 23 February 2009 have been fully considered but they are not persuasive.

Applicant argues that the additional reference does not overcome the alleged deficiencies of the first 35 U.S.C. 103 Rejection. As set forth above, the cited combination of references of Bruchez et al. and Mahamuni et al. teaches all of the limitation of the claims, therefore this argument is not persuasive.

Conclusion

No claim is allowed.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Papers related to this application may be submitted to Technical Center 1600 by facsimile transmission. Papers should be faxed to Technical Center 1600 via the central PTO Fax Center. The faxing of such pages must conform with the notices published in the Official Gazette, 1096 OG 30 (November 15, 1988), 1156 OG 61 (November 16, 1993), and 1157 OG 94 (December 28, 1993)(See 37 CFR § 1.6(d)). The Central PTO Fax Center Number is (571) 273-8300.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Russell Negin, whose telephone number is (571) 272-1083. The examiner can normally be reached on Monday-Friday from 7am to 4pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's Supervisor, Marjorie Moran, Supervisory Patent Examiner, can be reached at (571) 272-0720.

Information regarding the status of the application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information on the PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

/RSN/
Russell S. Negin
29 May 2009

/Marjorie Moran/
Supervisory Patent Examiner, Art Unit 1631